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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/992,914	WATANABE ET AL.	
	Examiner	Art Unit	
	David H. Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,43 and 46-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 43* is/are allowed.

6)☒ Claim(s) *46-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the Amendment and Remarks filed on 12 September 2005.

2. Those rejections not specifically addressed in this Office action are withdrawn in view of Applicants' amendments to the claims.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

4. Claims 46-51 remain rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility. This rejection is repeated for the reason of record as set forth in the last Office action mailed 11 March 2005. Applicant's arguments filed 12 September 2005 have been fully considered but they are not persuasive.

Applicants argue that claims 46-51 recite defined amino acid sequences or specific nucleotide sequences that are one sequence that may encode the defined amino acid sequence, and that the nucleic acid sequences are those of the raffinose synthase cDNAs cloned from soybean, Japanese Artichoke and corn, as in Examples 7, 9 and 11 of the specification; the amino acid sequences are those obtained by translation of the CDNA sequences (page 22, last paragraph of the Response). Applicants argue that there is substantial evidence of record that one of ordinary skill in the art can distinguish a RFS enzyme from a STS enzyme solely on the basis of amino acid sequence, and that Applicants have previously provided phylogenetic analyses of

the amino acid sequence of RFSs and STSs and have established that the degree of sequence homology among RFSs and among STSs is significantly higher than the degree of homology between RFSs and STSs (page 23, 2nd paragraph of the Response). These arguments are not found to be persuasive. The Examiner has established the fact that at the time of Applicants' invention, only one other plant raffinose synthase "gene" was know in the art, that being from cucumber and disclosed in US Patent 6,166,292 (see Office action mailed 6 February 2002). It is unclear how Applicants at the time of filing could make an assumption of function of an encoded "enzyme" using sequence similarity without actually showing the expressed encoding nucleic acid actually produced a raffinose synthase at the time of the instant invention.

Applicants argue that as testified by Mr. Nagasawa, the identity of a protein as a raffinose synthase is readily established by analysis of its sequence in comparison to the sequences shown in the present sequences listing, especially by comparison to SEQ ID N0: 2, the identity of which as a raffinose synthase the Examiner does not challenge, and that the conclusion reached by Mr. Nagasawa is consistent with the text of the specification at page 23, lines 14-17 (page 24, 2nd paragraph of the Response and the Nagasawa Declaration filed under 37 CFR 1.132 on 12 September 2005). The Nagasawa Declaration is not deemed sufficient to overcome the instant rejection for the reasons of record in previous Office actions. Given the evolutionary relationship between raffinose synthase and stachyose synthase, even a local alignment would not adequately distinguish the two simply based on amino acid sequence because both

enzymes would have similar binding regions, and distinguishing characteristics are not described in the instant specification.

Applicants argue that given the amino acid sequence, and identification of any particular protein as a raffinose synthase by virtue of homology to SEQ ID NO:2 (and 4, 6 and 8), the present specification provides an assay for raffinose synthase activity. Applicants argue that it can hardly be said that testing of a protein for activity using a disclosed assay method is undue experimentation and one of ordinary skill in the art can readily determine if in fact any one protein having a defined amino acid sequence has the activity of combining a D-galactosyl group through an α(1-6) bond with a hydroxyl group attached to the carbon atom at position 6 of a D-glucose residue in a sucrose molecule that defines a raffinose synthase enzyme (page 24, 4th paragraph of the Response). These arguments are not found to be persuasive because it is not pursuant upon one of skill in the art to establish the utility of what Applicants claim. See *Brenner v. Manson*, 383 U.S. 519 (1966), which states "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field."

Claim Rejections - 35 USC § 112

5. Claims 48-77 remain rejected and claims 82-86 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 11 March 2005. Applicant's arguments filed 12 September 2005 have been fully considered but they are not persuasive.

Applicants argue that Wallach relates to a claim to any and all genes encoding a TNF cytotoxic activity, which claims are based on description of only the amino-terminal portion of the TNF protein, no DNA sequences were provided, nor was even any full-length protein sequence provided. Applicants argue that the Wallach panel decided that, on these facts, adequate description of any and all genes encoding a TNF cytotoxic activity was not provided. Applicants argue that on the other hand, in the present application at least two complete sequences of raffinose synthase genes are provided (i.e. SEQ ID NOS: 1 and 3), as are their translated amino acid sequences (SEQ ID NOS: 2 and 4), and the present specification lists several PCR primers that may be used to produce additional raffinose synthase genes from DNA of additional plants and this process and two working examples of it are described (as SEQ ID NOS: 5-8) (page 28, 1st and 2nd paragraphs of the Response). These arguments are not found to be persuasive because Applicants have not established the function of the amino acid sequences of SEQ ID NO: 6 or 8 either. The Examiner notes that claims 53-58, 61, 62, 64, 66, 70-72, 74 and 77 are directed to isolated nucleic acids and compositions comprising said isolated nucleic acids from laminaceous and

monocotyledonous plants encoding raffinose synthase only described by a possible method of making, wherein Applicants have not adequately described a single species of the genus claimed.

Applicants argue that the structure of a nucleic acid that is within the genus of the invention is defined by its ability to hybridize to a reference sequence, e.g. SEQ ID NO: 1 (or 3, 5 or 7) under conditions recognized by the art as being highly stringent, and the function of the nucleic acid that is within the invention is that it encodes a protein having the activity of producing raffinose by combining a D-galactosyl group through an α(1-6) bond with a hydroxyl group attached to the carbon atom at position 6 of a D-glucose residue in a sucrose molecule (paragraph spanning pages 28-29 of the Response). This argument is not found to be persuasive because Applicants have not described any structural features that define the claimed genus, hybridizing is a functional limitation. As previously pointed out, one of skill in the art would not have recognized such a functional feature, hybridization, to adequately describe a nucleic acid encoding a raffinose synthase in view of the close relationship of stachyose synthase enzyme.

Applicants argue that in the present instance, the state of the science regarding raffinose synthase genes, and technology for isolating nucleic acids from organisms, is considerably advanced compared to that state at the time the Lilly case and the guidelines demanding that the structure-function relationship of a protein be delineated in a specification, and that in the instant case, the invention is far along from a "wish" or "plan" for how to obtain nucleic acids encoding raffinose synthase from plants (page 30, 1st paragraph of the Remarks). This argument is not found to be persuasive for the

reasons of record. It is the Examiner's opinion that one of skill in the art would not have recognized that Applicants were in possession of isolated nucleic acids encoding raffinose synthase as broadly claimed. Applicants do not describe any structural feature(s) of the claimed raffinose synthases that would describe the genus of isolated nucleic acids as broadly claimed.

Applicants argue that the instant specification includes two complete coding sequences of raffinose synthase cDNAs from two different plant genera, and two nearly complete coding sequences from yet two more plant genera. Applicants argue that the specification also describes how to obtain the terminal portions of cDNA when these are missing and a commercially available kit for doing so (see e.g., page 37, lines 18-22), thus, regardless of whether the complete cDNA sequence is actually provided in the specification, there can be no doubt that the teachings of the specification place the public in "possession" of the complete sequences of four different raffinose synthase cDNAs from diverse plant genera (page 30, 2nd paragraph of the Response). This argument is not found to be persuasive for the reasons of record. The Examiner has addressed the issue of the putative raffinose synthase encoding nucleic acid in SEQ ID NO: 3 from soybean supra.

Applicant argue that it is not necessary for the specification to provide detailed description of particular domains of the raffinose synthase protein that provide for its enzymatic activity as one of ordinary skill in the art can readily obtain cDNA encoding the entire protein utilizing the teachings of the specification (paragraph spanning pages 30-31 of the Response). This argument is not found to be persuasive. See *Vas-Cath*

Inc. v. Mahurkar 1991 (CA FC) 19 USPQ2d 1111, 1115, which teaches that the purpose of the written description is for the purpose of warning an innocent purchaser, or other person using a machine, of his infringement of the patent; and at the same time, of taking from the inventor the means of practicing upon the credulity or the fears of other persons, by pretending that his invention is more than what it really is, or different from its ostensible objects, that the patentee is required to distinguish his invention in his specification.

6. Claims 46-77 remain rejected and claims 78-86 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 2, a chimeric nucleic acid comprising said isolated nucleic acid, a transformant comprising said chimeric nucleic acid, a plasmid comprising said nucleic acid, a host organism either a microorganism or plant comprising said plasmid and a method of metabolic modification of a plant comprising introducing said isolated nucleic acid, does not reasonably provide enablement for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 4, 6 or 8, or an isolated nucleic acid that hybridizes with a complement to said isolated nucleic acid isolated from any leguminous, lamiaceous or monocotyledonous plant. This rejection is repeated for the reason of record as set forth in the last Office action mailed 11 March 2005. Applicant's arguments filed 12 September 2005 have been fully considered but they are not persuasive.

Applicants argue that encoding raffinose synthases are distinguishable at the sequence identity level from nucleic acids encoding STSs or SIPs (page 32, 2nd

paragraph of the Response). Applicants argue that the specification teaches that a particular nucleic acid should be isolated by the methods disclosed, i.e. by amplification of nucleic acids obtained from plants or another organism, preferably using the primers disclosed in the application and nucleic acids from the target organism as a template, thus, even at this initial step, there is no "random" aspect to the experimentation. Following the teachings of the specification, specific PCR products will be obtained from organisms highly likely to express a raffinose synthase protein (page 33, 3rd paragraph of the Remarks). These arguments are not found to be persuasive. The *Wands* factors put forth by the Court takes into consideration the general skill of one in the art at the time of Applicants' invention. The Examiner has provided evidence that one of skill in the instant art would require more than sequence similarity as evidence of function, contrary to Applicants assertion. See Duggleby 1997 and Richmond *et al* 2000, Plant Physiology 124: 495-498, see paragraph spanning left and right column on page 497 (previously cited). In addition, the art teaches that raffinose synthase enzymes have high overall amino acid sequence homology with seed imbibition proteins and stachyose synthases, hence amino acid sequence similarity cannot be used to assert function (see Peterbauer *et al* 2002, Planta 215: 839-846, see page 840, left column and page 841, right column; previously cited). Peterbauer *et al* teaches that to distinguish between raffinose synthase and stachyose synthase, primers must be chosen to encompass a block of amino acids which is exclusively present in stachyose synthase (page 841, right column, 1st paragraph). Applicants have provided no

guidance on how to distinguish isolated nucleic acids encoding raffinose synthase from those encoding stachyose synthase.

Applicants argue that once a nucleic acid has been obtained, it is expressed in some organism, Example 7 of the specification demonstrates expression in E. coli, the expressed protein is then assayed for raffinose synthase activity as described in Example 2 of the specification (page 34, 1st paragraph of the Response). This argument is not found to be persuasive because one of skill in the art would have to have a reasonable expectation that what was isolated would encode a raffinose synthase enzyme, otherwise it would be undue trial and error experimentation.

Double Patenting

7. Claims 46, 47, 52, 53, 55 and 59-77 remain and claims 78-86 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 16-23 and 28-30 of copending Application No. 09/301,766. Applicants do not address this rejection in the Response filed on 12 September 2005. The instant provisional rejection remains.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Claims 6 and 43 are allowed.

10. Claims 46-86 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at (571) 272-0975. The fax telephone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.

DAVID H. KRUSE, PH.D.
PRIMARY EXAMINER

David H. Kruse, Ph.D.
23 November 2005

12. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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